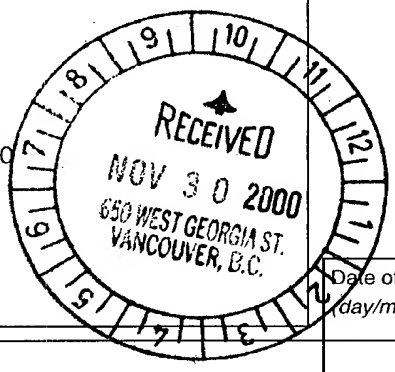
PATENT COOPERATION TREATY

From the
INTERNATIONAL PRELIMINARY EXAMINING AUTHORITY

To:

ROBINSON,J.Christopher
Smart & Biggar
Box 11560 Vancouver Centre
650 W. Georgia St., Suite 2200
Vancouver, BC V6B 4N8
CANADA



PCT

NOTIFICATION OF TRANSMITTAL OF THE INTERNATIONAL PRELIMINARY EXAMINATION REPORT
(PCT Rule 71.1)

Date of mailing *(day/month/year)*	23.11.2000
Applicant's or agent's file reference 80472-5	**IMPORTANT NOTIFICATION**

International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/CA99/00813	03/09/1999	03/09/1998

Applicant
THE UNIVERSITY OF BRITISH COLUMBIA et al.

1. The applicant is hereby notified that this International Preliminary Examining Authority transmits herewith the international preliminary examination report and its annexes, if any, established on the international application.

2. A copy of the report and its annexes, if any, is being transmitted to the International Bureau for communication to all the elected Offices.

3. Where required by any of the elected Offices, the International Bureau will prepare an English translation of the report (but not of any annexes) and will transmit such translation to those Offices.

4. **REMINDER**

The applicant must enter the national phase before each elected Office by performing certain acts (filing translations and paying national fees) within 30 months from the priority date (or later in some Offices) (Article 39(1)) (see also the reminder sent by the International Bureau with Form PCT/IB/301).

Where a translation of the international application must be furnished to an elected Office, that translation must contain a translation of any annexes to the international preliminary examination report. It is the applicant's responsibility to prepare and furnish such translation directly to each elected Office concerned.

For further details on the applicable time limits and requirements of the elected Offices, see Volume II of the PCT Applicant's Guide.

Name and mailing address of the IPEA/	Authorized officer
European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Danti, B Tel.+49 89 2399-8161

Form PCT/IPEA/416 (July 1992)

PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference	FOR FURTHER ACTION	See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)
80472-5		
International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/CA99/00813	03/09/1999	03/09/1998
International Patent Classification (IPC) or national classification and IPC C12Q1/68		
Applicant THE UNIVERSITY OF BRITISH COLUMBIA et al.		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 8 sheets, including this cover sheet.

   ☒ This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

   These annexes consist of a total of 6 sheets.

3. This report contains indications relating to the following items:

   - I ☒ Basis of the report
   - II ☐ Priority
   - III ☐ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
   - IV ☒ Lack of unity of invention
   - V ☒ Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations suporting such statement
   - VI ☐ Certain documents cited
   - VII ☒ Certain defects in the international application
   - VIII ☒ Certain observations on the international application

Date of submission of the demand	Date of completion of this report
07/02/2000	23.11.2000
Name and mailing address of the international preliminary examining authority: European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Authorized officer Herrero, M Telephone No. +49 89 2399 8542

Form PCT/IPEA/409 (cover sheet) (January 1994)

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/CA99/00813

I. Basis of the report

1. This report has been drawn on the basis of *(substitute sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to the report since they do not contain amendments (Rules 70.16 and 70.17).)*:
Description, pages:

1-8,12-14,16-20	as originally filed			
9-11,15	as received on	06/09/2000	with letter of	29/08/2000

Claims, No.:

1-5,6 (part)	as originally filed			
6 (part),7-17	as received on	02/09/2000	with letter of	25/08/2000

Drawings, sheets:

1/3-3/3	as originally filed

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

   These elements were available or furnished to this Authority in the following language: , which is:

   - ☐ the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).
   - ☐ the language of publication of the international application (under Rule 48.3(b)).
   - ☐ the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

   - ☐ contained in the international application in written form.
   - ☐ filed together with the international application in computer readable form.
   - ☐ furnished subsequently to this Authority in written form.
   - ☐ furnished subsequently to this Authority in computer readable form.
   - ☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
   - ☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

   ☐ the description, pages:

   ☐ the claims, Nos.:

   ☐ the drawings, sheets:

5. ☒ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)):

   (Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)
   see separate sheet

6. Additional observations, if necessary:
   see separate sheet

IV. Lack of unity of invention

1. In response to the invitation to restrict or pay additional fees the applicant has:

   ☐ restricted the claims.

   ☐ paid additional fees.

   ☐ paid additional fees under protest.

   ☐ neither restricted nor paid additional fees.

2. ☒ This Authority found that the requirement of unity of invention is not complied and chose, according to Rule 68.1, not to invite the applicant to restrict or pay additional fees.

3. This Authority considers that the requirement of unity of invention in accordance with Rules 13.1, 13.2 and 13.3 is

   ☐ complied with.

   ☒ not complied with for the following reasons:
   see separate sheet

4. Consequently, the following parts of the international application were the subject of international preliminary examination in establishing this report:

   ☒ all parts.

   ☐ the parts relating to claims Nos. .

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	1-17
	No:	Claims	
Inventive step (IS)	Yes:	Claims	1-16
	No:	Claims	17
Industrial applicability (IA)	Yes:	Claims	1-17
	No:	Claims	

2. Citations and explanations
see separate sheet

VII. Certain defects in the international application

The following defects in the form or contents of the international application have been noted:
see separate sheet

VIII. Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:
see separate sheet

SECTION I

3. The amendments filed with the letter dated 25.08.00 introduce (apparently by mistake) subject-matter which extends beyond the content of the application as filed, contrary to Article 34(2)(b) PCT. The amendments concerned are the following: the genomovar-specific primer pairs cited in the newly filed Claim 14, which are not supported by the corresponding disclosure on pages 7-9.

   Accordingly, Claim 14 as originally filed has been taken into account for the purposes of the present preliminary examination report.

4. Additional observations

   This preliminary examination report also takes into consideration pages 1/15 to 15/15 of the Sequence Listing (i.e. information concerning SEQ ID NOs 1 to 40).

SECTION IV

The subject-matter presently claimed can be clearly divided into the following separate inventions/groups of invention:

(1) Claims 1-16 (first invention): methods for the identification and speciation of bacteria belonging to the *Burkholderia cepacia* complex (Claims 1-7). Reagents (i.e. compositions comprising a suitable pair of polynucleotide primers according to Claims 8-10 and 13-14) and kits (Claims 11-12 and 15-16) for use in the methods of Claims 1-7.

(2) Claim 17 (second invention): vaccine composition for the treatment and prevention of infection with epidemic bacteria (belonging to genomovar III) of the *Burkholderia cepacia* complex comprising flagellin or a flagellin-derived antigen or a polynucleotide encoding flagellin or a flagellin-derived antigen.

It is *a priori* apparent that no single general inventive concept links the subject-mater of Claims 1-16 (first invention) to Claim 17 (second invention), contrary to the requirements of Rule 13.1 PCT.

Moreover, there is also no technical relationship among the methods, reagents and kits encompassed by Claims 1-16 and the vaccine composition of Claim 17 involving one or more of the same or corresponding special technical features that define a contribution which each of the claimed inventions, considered as a whole, makes over the prior art and therefore the requirements of Rule 13(2) PCT are not complied with.

SECTION V

2. CITATIONS AND EXPLANATIONS

2.1 The following document has been considered for the purposes of this report:

D1: Vandamme, P. et al (1997) Int. J. Syst. Bacteriol. **47**:1188-1200 (also cited in the application).

As mentioned on page 1 of the present application, it has been shown in D1 that the Gram negative bacterium *Burkholderia cepacia* actually consists of five different genomovars (or new species). Two of these genomovars have been given new species names, namely *Burkholderia multivorans* (formerly genomovar II) and *Burkholderia vietnamensis* (formerly genomovar V). As a collective, these two species together with *Burkholderia cepacia* genomovar I, *Burkholderia cepacia* genomovar III and *Burkholderia cepacia* genomovar IV have been designated as the *B. cepacia* complex.

2.2 The present application discloses a seemingly rapid procedure suitable for the identification and speciation of bacteria belonging to the *B. cepacia* complex present in a sample, which relies on the information provided by a *rec*A gene-based PCR assay. The application shows, in particular, that the described

process of speciation of *B. cepacia* bacteria based upon RFLP (restriction fragment length polymorphism) analysis of PCR-amplified *rec*A gene is highly discriminatory and demonstrates that the approach of the invention will clearly distinguish between all five of the current genomovars and also newly defined groups within the *B. cepacia* complex, i.e. the two sub-groups designated as RG-A and RG-B within genomovar III (cf page 6, lines 18-25).

(1) First invention: Claims 1-16

In the light of the available prior art the hereby claimed methods for the identification and speciation of bacteria belonging to the *Burkholderia cepacia* complex (Claims 1-7), compositions comprising pairs of primers for amplification (Claims 8-10 and 13-14) and speciation kits (Claims 11-12 and 15-16) would appear to relate to novel and inventive subject-matter susceptible of industrial applicability and therefore to satisfy the criteria set forth in Art. 33(2)(3) and (4) PCT.

(2) Second invention: Claim 17

Regarding the intended vaccine composition according to Claim 17 it is emphasized that no experimental support is found elsewhere in the application as originally filed on the basis of which it could be established that the expected technical effects, e.g. prevention of infection, are indeed obtained and thus is not possible to assess that the claimed subject-matter involves an inventive step (Art. 33(3) PCT).

The arguments put forward by the Applicants have been considered, however, the present Examining Authority is still of the opinion that the explanations given in the supporting description aimed at substantiating that the encoded protein (the product of the flagellin gene of *Burkholderia cepacia* genomovar III strains) is suitable for use as an antigen for development of vaccines against the most problematic strains in patients with cystic fibrosis (CF), are merely of a predictive and speculative nature (see in particular page 11, lines 9-11 and 19-21). Conversely, no information is available substantiating, for instance, the protection

of animals immunized with a composition comprising the flagellin antigen of interest against challenge with an infective strain belonging to the epidemic *Burkholderia cepacia* genomovar III.

SECTION VII

The expression "incorporated herein by reference" in respect of prior art documents on page 12, line 22 leads to a doubt as to whether the requirements of the description being self-contained are satisfied (see PCT Guidelines C-II, 4-17).

SECTION VIII

In the light of the supporting description (see page 4, lines 21-31 bridging over page 5, lines 1-11) it is evident that the composition comprising the pair of primers identified in present dependent Claim 9 is useful to carry out a non-specific PCR amplification of the *rec*A gene, i.e. said pair of primers is effective to amplify substantially the entire *rec*A gene from all known members of the *B. cepacia* complex.

In view of the foregoing, the intended composition according to dependent Claim 9 cannot be regarded as a composition suitable for the production of a diagnostic amplicon from the *rec*A gene as defined in independent Claim 8. The subject-matter encompassed by Claim 9 is therefore inconsistent with the definition of the composition of the invention according to Claim 8, contrary to Art. 6 PCT.

This deficiency (Art. 6 PCT) affects *mutatis mutandis* the subject-matter of appended Claims 11 and 12, insofar as these claims rely in part on the pair of primers in accordance to present Claim 9.